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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,435	10/21/2003	Mark F. Pittenger	640100.470	3718

7590 03/22/2007

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,435	PITTENGER ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-10 and 12-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-10 and 12-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/24/06 & 1/8/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Applicants' response of December 26, 2006, to the non-final action dated September 22, 2006 has been entered. Claims 1, 4, 12 and 17 have been amended. No claims were cancelled or newly added. Claims 1-2, 4-10 and 12-21 are pending in the application and under current examination.

New Claim Objection under 37 CFR § 1.121

Claims 1 and 4 are newly objected to, under 37 CFR § 1.121 (c) for containing incorrect status identifiers. Claims 1 and 4 are currently amended, but have been identified as (Previously presented). Appropriate correction of the claim status identifiers is required.

Applicants should note that the submission of any further defective amendments will results in a notice of non-compliant amendment.

Claims 16 and 21 are newly objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 16 and 21 depend from claims 12 and 17 respectively and recite that the mesenchymal stem cells are allogeneic, thus failing to further limit the base claims.

Response to Claim Rejections - 35 USC § 112- Second Paragraph

Claims 1-2, 4-10 and 12-21 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The rejection set forth on pp. 2-3 of the previous office action dated September 22, 2006 is maintained in part for claims 1-2, 4-10 and 12-21 for reasons of record. Applicants' amendment of claims 1, 4, 12 and 17, adding essential steps, partially obviates the previous ground of rejection.

Applicants disagree with the rejection, asserting that the specification states that mesenchymal stem cells (MSCs) can be administered by a variety of procedures and Lee et al. (of record) state that "Transplanted stem cells also undergo a "homing" process in which they are

attracted to the site of injury" [column 2, lines 26-28], and those skilled in the art, when reading the specification, would understand readily that, if administered systemically, the mesenchymal stem cells will travel to the heart in order to produce cardiomyocytes or blood vessels of the heart, thereby improving ventricular wall motion, repairing or regenerating blood vessels, or stimulating or promoting angiogenesis in the heart. Applicants' arguments have been fully considered, but are not found persuasive.

The issue is how the administration of MSCs by any route (or intravenously) would produce cardiomyocytes or promote angiogenesis limited to the heart to an individual. For example, an intradermal delivery of MSCs is unlikely to produce cardiomyocytes in the heart.

Regarding systemic or intravenous administration (claim 1), it appears that the teachings of Lee et al. are taken out of context. Lee et al. teach that regeneration of cardiomyocytes may be attained by mobilizing bone marrow resident stem cells to the site of injury with the use of cytokines such as granulocyte colony stimulating factor, by a homing mechanism that is not clearly understood, (second column, p. 729), or by an indirect approach where MSCs which were mobilized by systemic injections of cytokines (such as GMCSF and stem-cell factor) homed to the infracted myocardium (pp. 729-730, bridging). The instant claims are not directed to bone marrow resident stem cells and further do not recite the mobilization of MSCs by systemic injections of cytokines.

It is therefore maintained that the claims should recite: "administering to the heart of an individual", to be consistent with the preamble of the claims.

Thus, the rejection of claims 1-2, 4-10 and 12-21 is maintained for reasons of record and the foregoing discussion.

Response to Claim Rejections - 35 USC § 112-Scope of Enablement

Claims 12-21 stand rejected under 35 U.S.C.§112, first paragraph, because the specification lacks an enablement for the full scope of the claimed invention. The rejection set forth on pp. 3-7 of the previous office action dated September 22, 2006 is maintained in party for claims 12-21, for reasons of record. Applicants' amendment of claims 12 and 17, identifying MSCs as autologous or allogeneic, partially obviates the previous ground of rejection.

Applicants traverse the rejection, asserting the examples show that MSCs did contribute to the formation of blood vessels in the heart. Referring to Examples 6 and 7 of the specification, Applicants state that MSCs were found surrounding, and associated with blood vessels of the heart. The MSCs were localized within a blood vessel, and associated with the smooth muscle layer of the vessel and expressed Factor VIII and VEGF. Applicants' arguments have been fully considered, but are not found persuasive.

In response, it is maintained that the specification does not show the production of any vascular cell, or any evidence for the formation of arteries, veins and capillaries, formed as a result of administering MSCs to the heart. Localization and association with the smooth muscle layer is not synonymous with repair or regeneration of blood vessels or the promotion of angiogenesis, as the amount or sufficiency of the expressed factors cannot be determined. Therefore, it remains unclear whether transplanted adult MSCs of the instant invention resulted in the repair and regeneration of blood vessels, as even the indirect contribution of the MSCs in providing angiogenesis promoting factors cannot be determined in an environment where such factors are continually supplied by various cells and tissues.

Applicants cite *Ex parte Mark*, and argue that Applicants need not show that every embodiment within the scope of a claim must be operable in order for the claim to be valid. Such is not persuasive, because the subject matter in *Ex parte Mark* was directed to cysteine-depleted muteins of biologically active proteins and is thus not on point. Further, the allogeneic MSCs in Example 7 were transplanted by direct injection into infracted pig hearts, and not administered by other means. Additionally, the working example does provide an enablement for formation of blood vessels or angiogenesis, and moreover, a single embodiment does not overcome the art recognized unpredictability for the genus encompassed by the claims. As also indicated in MPEP 2164.03, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938).

Therefore, it is maintained that the specification does not provide an enabling disclosure for repairing or regenerating blood vessels, or a method of stimulating or promoting angiogenesis in the heart of an individual, or where MSCs (or genetically modified MSCs) are administered by any route to said individual.

Thus, the rejection of claims 1-2, 5-13, 22-27 and 49-57 is maintained for reasons of record and the foregoing discussion.

Conclusion

Claims 1-2, 4-10 and 12-21 are not allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

Fereydoun G. Sajjadi, Ph.D.
Examiner, USPTO, AU 1633

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER